CLAIMS

[Claim(s)]
[Claim 1] The manufacturing method of the granular covering pharmaceutical preparation which is the manufacturing method of the granular covering pharmaceutical preparation which comes to cover the particle which contains [two or more sorts of support] a drug for the melting point of this support in high order, and includes the following processes at least.
a) The process which cools and obtains single covering pharmaceutical preparation after mixing the particle containing a drug with support with the highest melting point at the temperature more than this melting point among two or more sorts of support.
b) The process which cools and obtains duplex covering pharmaceutical preparation after mixing the single covering pharmaceutical preparation obtained by a at the temperature of more than the high melting point and under the highest melting point to the 2nd of support with the 2nd highest melting point, and two or more sorts of support of two or more sorts of support.
c) The process cooled and covered after support furthermore mixes next three or more kinds of duplex covering pharmaceutical preparation obtained by b at the temperature of under the melting point of support with the high melting point, and the support covered more than the melting point of that support, and just before in a certain case, the process which performs this process repeatedly if needed one by one below.
[Claim 2] The manufacture approach according to claim 1 that the melting point of two or more sorts of support is 40 degrees C - 90 degrees C.
[Claim 3] The manufacture approach according to claim 1 or 2 that the difference of the melting point of two or more sorts of support is 10 degrees C or more respectively.
[Claim 4] The manufacture approach according to claim 1 to 3 that two or more sorts of support is water-insoluble nature.
[Claim 5] The manufacture approach according to claim 1 to 4 that two or more sorts of support is fats and oils.
[Claim 6] The manufacture approach according to claim 1 to 5 that support is two sorts, castor bean hardened oil and rapeseed hardened oil.
[Claim 7] The manufacture approach according to claim 1 to 6 that all the particle diameter of the particle after support covering is 850 micrometers or less, and a thing 500 micrometers or more is [a thing (5% or less of total weight and 75 micrometers or less)] 10% or less.
[Claim 8] The manufacture approach according to claim 1 to 7 that the total amount of covering of support is the 10 - 110 weight section to the particle 100 weight section containing a drug.
[Claim 9] The manufacture approach according to claim 1 to 8 which is the drug with which a drug presents the unpleasant taste.
[Claim 10] The manufacture approach according to claim 9 that the unpleasant taste is bitterness [claim 11] The manufacture approach according to claim 1 to 8 of coming to choose a drug from rokitamycin, milnacipran hydrochloride, and hydrochloric-acid ceftizoxime ARAPIBOKISHIRU.
[Claim 12] A drug is hydrochloric-acid ceftizoxime ARAPIBOKISHIRU and it is Japanese

pharmacopoeia General Test Procedures. Dissolution test The manufacture approach according to claim 1 to 8 characterized by eluting 75% or more of the content of a drug in 30 minutes in the 2nd law.
[Claim 13] Granular covering pharmaceutical preparation which is the granular covering pharmaceutical preparation which comes to cover the particle which contains a drug for two or more sorts of support in order with the high melting point of this support, and can be manufactured through the following processes at least.
a) The process which cools and obtains single covering pharmaceutical preparation after mixing the particle containing a drug with support with the highest melting point at the temperature more than this melting point among two or more sorts of support.
b) The process which cools and obtains duplex covering pharmaceutical preparation after mixing the single covering pharmaceutical preparation obtained by a at the temperature of more than the high melting point and under the highest melting point to the 2nd of support with the 2nd highest melting point, and two or more sorts of support of two or more sorts of support.
c) The process cooled and covered after support furthermore mixes next three or more kinds of duplex covering pharmaceutical preparation obtained by b at the temperature of under the melting point of support with the high melting point, and the support covered more than the melting point of that support, and just before in a certain case, the process which performs this process repeatedly if needed one by one below.
[Claim 14] Pharmaceutical preparation according to claim 13 whose support is two sorts, castor bean hardened oil and rapeseed hardened oil.
[Claim 15] Pharmaceutical preparation given in either of claims 13 or 14 to which it comes to choose drugs from rokitamycin, milnacipran hydrochloride, and hydrochloric-acid ceftizoxime ARAPIBOKISHIRU.

[Translation done.]

DETAILED DESCRIPTION

[Detailed Description of the Invention]
[Field of the Invention]
[0001] This invention relates to the manufacture approach of granular covering pharmaceutical preparation of making hard to be influenced effect on the drug from an external environment, and improving unpleasant tastes, such as bitterness, a pungent condiment, and sweet taste, and improving recipe nature, and its granular covering pharmaceutical preparation, by covering the particle containing a drug.
[0002]
[Description of the Prior Art] Granular pharmaceutical preparation, such as dry-syrups with a large specific surface area, powder, and a fine grain agent, tends to be influenced from an external environment, and is sensitive in the taste, and recipe nature gets very bad when a drug has an unpleasant taste (bitterness, a pungent condiment, an astringent taste, and an unpleasant smell are included). Especially, the problem of compliance, such as medication difficulty, occurs in the pharmaceutical preparation for children. Although dry-syrups and a fine grain agent are chosen from the simplicity of a formula and recipe as dosage forms for children in many cases, there is little what has controlled exsorption of the unpleasant taste of a drug enough, and the present condition is adding and carrying out taste masking of perfume or the sweetners.
[0003] Conventionally, in drugs, the approach of covering a high polymer on the surface of a particle is learned as an approach of making the taste of the matter which has an unpleasant taste mitigating. For example, when using water soluble polymer matter, such as hydroxypropylcellulose, and a drug is easily dissolvable in water, as for infiltration of the drug to a covering film front face, and a drug unstable in water, the fall of activity may take place. moreover, the case where water-insoluble nature high polymers, such as ethyl cellulose, are used -- an organic solvent -- using it (JP,2-96516,A) -- a masking effect may worsen by shift of the drug to the inside of a solvent, and even if it considers use of an organic solvent from the field of effect by the environment, it has danger, such as explosion and ignition, preferably. Moreover, since the adhesion in inner mouth is accompanied by the feeling of a rough deposit from the configuration also in a water-insoluble nature high polymer when using the water soluble polymer matter, neither has desirable recipe nature.
[0004] In order to solve these problems in recent years, the approaches (JP,1-287021,A, JP,2-96516,A, JP,4-300821,A, etc.) of cooling back and covering which carried out melting were developed by heat-treating the low-melt point point matter on a particle front face. However, if it is going to heighten a masking effect also by this approach, contact of the interior of a coat and the exterior must be controlled as much as possible, therefore a covering part becomes thick, and there are problems, such as needing the low-melt point point matter for a large quantity as a result, or having a bad influence on the quality of products, such as elution delay and an increment in an aggregate. Therefore, the present approach of coexistence of quality and masking is inadequate.
[0005]
[Problem(s) to be Solved by the Invention] It is the purpose to offer the manufacture approach of

granular covering pharmaceutical preparation that this invention was excellent in recipe nature, prompt elution was moreover shown and absorption in the living body was also excellent.

[0006]

[Means for Solving the Problem] In order to solve said technical problem, as a result of inquiring wholeheartedly, this invention person is the manufacturing method of the granular covering pharmaceutical preparation which comes to cover the particle which contains [two or more sorts of support] a drug for the melting point of this support in high order, and found out the manufacturing method of the granular covering pharmaceutical preparation which includes the process of the following ab at least.

a) The process which cools and obtains single covering pharmaceutical preparation after mixing the particle containing a drug with support with the highest melting point at the temperature more than this melting point among two or more sorts of support.

b) The process which cools and obtains duplex covering pharmaceutical preparation after mixing the single covering pharmaceutical preparation obtained by a at the temperature of more than the high melting point and under the highest melting point to the 2nd of support with the 2nd highest melting point, and two or more sorts of support of two or more sorts of support.

c) The process cooled and covered after support furthermore mixes next three or more kinds of duplex covering pharmaceutical preparation obtained by b at the temperature of under the melting point of support with the high melting point, and the support used more than the melting point of that support, and for just before in a certain case, the process which performs this process repeatedly if needed one by one below.

[0007] It is desirable for the melting point to choose two or more kinds of support pharmacologically permissible at 40-90 degrees C, to carry out melting mixing of them at order with the high melting point, to repeat to cover the front face of said particle in order, and to cool to the particle containing a drug, and to obtain granular covering pharmaceutical preparation to it in this invention. As for especially the difference of the melting point of two or more kinds of support, it is respectively desirable to make it 15 degrees C or more 10 degrees C or more. Moreover, when that the total amount of covering of support is the 10 - 110 weight section forms two or more little enveloping layers desirably to the particle 100 weight section containing a drug, granular covering pharmaceutical preparation with a smooth front face is obtained with sufficient masking effect and particle diameter moderate although taken. That is, in case this invention covers the granulation object containing the drug which has an unpleasant taste and manufactures granular covering pharmaceutical preparation, it uses for order with the high melting point two or more kinds whose melting points are 40 degrees C - 90 degrees C of pharmacologically permissible support, and manufactures the granular covering pharmaceutical preparation with which the unpleasant taste including the process which repeats carrying out melting mixing and covering this support has been improved.

[0008] Furthermore, as for this support, it is desirable that it is water-insoluble nature, and it is desirable to specifically use fats and oils especially castor bean hardened oil, and rapeseed hardened oil. Moreover, the whole of the particle diameter is 850 micrometers or less, and, as for the particle after support covering, it is desirable for a thing 500 micrometers or more to be [for a thing (5% or less of total weight and 75 micrometers or less)] 10% or less. Rokitamycin, milnacipran hydrochloride, hydrochloric-acid ceftizoxime ARAPIBOKISHIRU, etc. are used for the drug and concrete target which present the taste unpleasant as these drugs, especially bitterness. When especially a drug is hydrochloric-acid ceftizoxime ARAPIBOKISHIRU, it is desirable that it is that in which 75% or more of the content of a drug is eluted in 30 minutes in the 2nd law of a Japanese pharmacopoeia General Test Procedures elution test.

[0009] Moreover, this invention relates to the granular covering pharmaceutical preparation which covers with support the granulation object containing the drug which has an unpleasant taste, and is obtained. The covered enveloping layer by the pharmacologically permissible support whose melting point is 40 degrees C - 90 degrees C is formed more than two-layer, and this granular covering pharmaceutical preparation is granular covering pharmaceutical preparation with which the unpleasant

taste characterized by using low support has been improved from support with the high melting point in order of the enveloping layer of an inside enveloping layer to an outside. Moreover, the pharmaceutical preparation obtained by this invention not only takes effect, but shows effectiveness to stabilization of drugs, gradual-release-izing, and selection of an elution part to the improvement of the unpleasant taste. If it is hygroscopic high drugs and is the drugs disassembled according to moisture absorption, decomposition can be prevented by considering as the granular covering pharmaceutical preparation by the support of water-insoluble nature by this invention. Moreover, gradual-release-izing and selection of an elution part are also possible by choosing the support which is hard to be decomposed into the digestive juices of a specific organ.

[0010]

[Embodiment of the Invention] This invention is explained concretely below. Although it will not be limited especially if it becomes a solid in dryness as a drug of this invention, what has a desirable unpleasant taste (bitterness, a pungent condiment, an astringent taste, and an unpleasant smell are included), what has desirable gradual-release-izing are mentioned. concrete -- a CNS drug (aspirin and meclofenoxate hydrochloride --) Chlorpromazine, tolmetin sodium, milnacipran hydrochloride, phenobarbital, etc., the medicine for systema nervosum periphericum (etomidoline, tolperisone hydrochloride, and pipethanate ethobromide --) cardiovascular preparation (aminophylline --), such as methylbenactyzium bromide and flopropion medicine for respiratory organs (ephedrine hydrochloride --), such as etilefrine hydrochloride, diltiazem hydrochloride, digitoxin, and captopril Clorprenaline hydrochloride, oxeladin citrate, cloperastine, disodium cromoglycate, etc., a gastrointestinal (berberine chloride, loperamide hydrochloride, cimetidine, and sennoside --) vitamin compounds (an ascorbic acid and cetotiamine hydrochloride --), such as dehydrocholic acid Cocarboxylase, calcium pantothenate, riboflavin tetrabutyrate, etc., the medicine for metabolic pharmaceutical preparation (camostat mesilate, mizoribine, lysozyme chloride, etc.) allergy (cyproheptadine hydrochloride --) Diphenhydramine hydrochloride, alimemazine tartrate, suplatast tosilate, chemotherapic drugs (aciclovir and enoxacin --), such as maleic-acid diphenhydramine antibiotic preparations (an erythromycin --), such as ofloxacin, pipemidic acid trihydrate, and levofloxacin Cefcapene pivoxil hydrochloride, cefteram pivoxil, cefpodoxime proxetil, Cefaclor, clarithromycin, rokitamycin, Are shown by hydrochloric-acid ceftizoxime ARAPIBOKISHIRU. () [Pivaloyloxymethyl-[] 6R, (R[7])-7-[(Z) -2-[(S) -alanylamino]-4-thiazolyl]-2-methoxyiminoacetamido]-8-oxo-5-thia-1-azabicyclo[4, 2 and 0]oct-2-ene-2-carboxylatehydrochloride(s) (JP,6-102667,B etc.) are mentioned. Furthermore, in such a drug, what [especially] is unstable as matter is desirable under soluble or existence of water in water.

[0011] Since a drug is usually a particle, once corning by a certain approach is desirable. Additives for physic, such as an excipient, a buffer, disintegrator, and a binder, may be added if needed. What is necessary is to just be based on the usual addition and the addition approach, in adding the additive for physic. As the approach of a granulation, generally, although dry granulation, wet granulation, etc. are mentioned, an approach is not limited but a granulation object just obtains the target particle diameter. The mean particle diameter of a final product (granulation object after covering) 100 micrometers - about 1000 micrometers, Preferably The specification of the powder of 14th revised Japanese Pharmacopoeia (there is no particle 850 micrometers or more, and a particle 500 micrometers or more is 5% or less of total weight), Furthermore, since it aims at particle diameter which suits the specification (the specification of powder is suited and a particle 75 more micrometers or less is 10% or less of total weight) of the fine grain agent of 14th revised Japanese Pharmacopoeia preferably, as for the mean particle diameter of a granulation object, 50 micrometers - about 400 micrometers are illustrated.

[0012] The melting point of this invention is not limited especially as pharmacologically permissible support which is 40 degrees C - 90 degrees C. If the effect of the workability and drug on manufacture is taken into consideration, it is desirable that it is 90 degrees C or less, and when these melting points consider the preservation gestalt of a product, it is desirable that it is at least 40 degrees C or more. Specifically For example, castor bean hardened oil (melting point = the inside of 86 degrees C and a following parenthesis shows the melting point), Various hardened oil, such as soybean hardened oil (67 degrees C) and rapeseed hardened oil (68 degrees C); Stearyl alcohol (59 degrees C), Higher alcohol,

such as cetanol (50 degrees C); Stearin acid (69 degrees C), Higher fatty acids, such as a palmitic acid (56 degrees C); A carnauba wax (86 degrees C), It exposes. Hydrocarbon; macrogol 4000s, such as vegetable properties, such as beeswax (67 degrees C), animal fat, or low; paraffin (50-70 degrees C) (55 degrees C), Polyethylene glycols, such as macrogol 6000 (59 degrees C); surfactants, such as higher-fatty-acid monoglyceride, such as sucrose fatty acid ester (40-60 degrees C) and glyceryl monostearate (60 degrees C), and a polyoxypropylene glycol (40-60 degrees C), are mentioned. Preferably, it is the water-insoluble nature matter, and the melting point which cannot be easily temperature influenced of [at the time of preservation] is 60 degrees C - 90 degrees C, and castor bean hardened oil excellent in the plasticity of the liquid at the time of melting, rapeseed hardened oil, a carnauba wax, etc. are illustrated especially.

[0013] Although ********** [the number of it / what] as long as the support which the melting point used in this invention can permit pharmacologically at 40 degrees C - 90 degrees C is two or more kinds, it is desirable that it is separated from at least 10 degrees C or more of each temperature gradient. For example, castor bean hardened oil, rapesced hardened oil (18 degrees C of melting point differences), a carnauba wax and stearyl alcohol (27 degrees C of melting point differences), stearin acid, cetanol (19 degrees C of melting point differences), etc. are illustrated as a desirable combination.

[0014] The addition approach of such support for the granulation object containing a drug is illustrated as an example with the desirable approach of usually mixing, while warming support in a granulation object, although a proper approach can be used. Although support may be added according to which condition of fine particles or a liquid on the occasion of addition of support, if the simplicity of a process is taken into consideration, addition by fine particles is desirable. Although what is necessary is just to carry out whenever [warming or stoving temperature] more than the melting point of support, extent higher about 5-10 degrees C than the melting point of support and desirable temperature high about 10 degrees C are usually illustrated. Melting of the support is carried out with heating, and it covers, and it is covered with cooling after that (room temperature extent) when support forms a substantial layer (enveloping layer). However, in case those support is covered, effectiveness sufficient in combination which is fused when the matter covered first covers later is not acquired. That is, by forming two or more enveloping layers of the layer covered first and the layer covered from the back, masking effect sufficient by little addition can be acquired. Therefore, since the melting point of the first support is an elevated temperature more and the temperature control at the time of such a clear clothing layer that combination [as / whose melting point of next support is low temperature more] being desirable and the difference of both melting point being large being easy to be formed, and carrying out melting processing of the support of the melting point by the side of low temperature is also easy, the combination of about 10 degrees C of melting point differences which were mentioned above is desirable. A melting point difference 20 degrees C or more is most preferably desirable 18 degrees C more preferably 15 degrees C still more preferably. In addition, covering to support and coincidence is also possible except matter which checks coat formation.

[0015] The addition (it is called the amount of covering below) of the support which covers a granulation object in this invention will not be restricted especially if it is the minimum amount which covers a granulation object. However, since the amounts of covering which mask the unpleasant taste with the surface area of a particle differ, as an amount which attains uniform covering thickness, more than the amount of covering 10 weight section is desirable [the amounts] to the granulation object 100 weight section. In order that the elution nature of a drug may avoid getting extremely bad by covering, however, in hydrochloric-acid ceftizoxime ARAPIBOKISHIRU the Japanese pharmacopoeia General Test Procedures 2nd law Dissolution test (a paddle method --) The amount of covering to which 75% or more of the content of a drug is eluted in 30 minutes according to paddle rotational frequency 50 rotation in the buffer solution (it is 37 degrees C whenever [pH 1.2 / about / and solution temperature] with the liquid which melted dilute-hydrochloric-acid 24.0mL and water to 2.0g of sodium chlorides, and was set to 1000mL(s)) of 900mL(s) is desirable. Moreover, since particle diameter will become large and feeling of recipe, such as a rough deposit, will worsen if the amount of covering increases, below 30 weight sections are especially preferably usually desirable below the 110 weight sections to

the granulation object 100 weight section.
[0016] The manufacture approach of the granular covering pharmaceutical preparation of this invention can be performed by the following approaches. First, a drug and various additives are mixed and corned and the particle containing a drug is obtained. The particle size of the particle containing this drug has desirable 50-400 micrometers. the inside of the particle containing this drug, and two or more sorts of support -- support with the highest melting point -- warming -- it warms to temperature higher 5-10 degrees C than the melting point of this support, supplying to the agitation granulation in a plane which has a function, and mixing, and single covering pharmaceutical preparation is obtained by returning and cooling to a room temperature after checking that the front face of the particle which melting is fully carried out and contains a drug has adhered at homogeneity. Under the present circumstances, if the agitation granulation machine is beforehand warmed to the above-mentioned temperature, it can cover in a short time. Subsequently, support with the high melting point is mixed with this single covering pharmaceutical preparation by the agitation granulation in a plane to the degree of the aforementioned support. Although the highest support of the melting point does not have ****, next the support with the high melting point ****** temperature. That is, it warms among two or more sorts of support to the temperature of more than the melting point high to the 2nd, and under the highest melting point, and secondary coating pharmaceutical preparation is obtained by returning and cooling to a room temperature after checking that melting of the support of the melting point high to the 2nd was fully carried out, and single covering pharmaceutical preparation has adhered at homogeneity. If the agitation granulation machine is beforehand warmed also in this case, it can cover in a short time. Moreover, still higher order covering pharmaceutical preparation may be obtained if needed. In this case, particle shape is further arranged using a dust size selector. Finally the various additives usually used as an excipient are added, and granular covering pharmaceutical preparation is obtained.
[0017] Specifically in this invention, dry-syrups, powder, a fine grain agent, etc. are illustrated as granular covering pharmaceutical preparation.
[0018]
[Example] This invention is not limited by the example although this invention is concretely explained based on an example.
[0019]
[Example 1] The hydrochloric-acid ceftizoxime ARAPIBOKISHIRU 30 weight section (a drug, thing which **(ed) according to the approach given in JP,6-102667,B), the precipitated-calcium-carbonate 30 weight section (Bihoku Funka Kogyo CO., LTD. make), and the crystalline cellulose 40 weight section (the Asahi Chemical Co., Ltd. make, trade name Avicel PH-101) were mixed, the after [granulation] particle size regulation was carried out with the dry type granulating machine (the Freund Industrial make, trade name TF-MINI), and it considered as the granulation object with a particle diameter of about 200 micrometers. It heat-treated at about 95 degrees C, having added the castor bean hardened-oil (Freund Industrial make, trade name Lubri wax101, melting point of 86 degrees C) 10 weight section to this granulation object 90 weight section, and mixing slowly in an agitation granulation machine (Powrex Make, trade name FM-VG -01), and cooling processing was carried out by taking out from an agitation granulation in a plane, and carrying out room temperature neglect after checking that melting was carried out enough and the granulation object has adhered at homogeneity. Furthermore, it heat-treated at about 75 degrees C, mixing slowly rapeseed hardened oil (the Freund Industrial make, a trade name Lubri wax 103, and melting point of 68 degrees C) to this granulation object 90 weight section covered once by 10 weight sections, in addition the agitation granulation in a plane, and cooling processing was carried out by taking out from an agitation granulation in a plane, and carrying out room temperature neglect after checking that melting was carried out enough and the granulation object has adhered at homogeneity. A particle size regulation is carried out in the mesh of a 500-micrometer opening after that, and it considers as granular covering pharmaceutical preparation, and is optimum dose ****** further about Aspartame (Ajinomoto Co., Inc. make) and magnesium aluminometasilicate (the product made from Fuji Chemistry, trade name noy SHIRIN UFL2). (the granulation object 100 weight section -- receiving -- the amount of covering of the about 23 weight section, 0% of particle

diameter of 850 micrometers or more and 0% 500 micrometers or more, and 1% 75 micrometers or less, and mean-particle-diameter =260micrometer)

[0020]

[Example 2] The hydrochloric-acid ceftizoxime ARAPIBOKISHIRU 30 weight section, the precipitated-calcium-carbonate 15 weight section, the citric-acid 3 sodium (Showa Kako Corp. make) 15 weight section, and the crystalline cellulose 40 weight section were mixed, the after [granulation] particle size regulation was carried out with the dry type granulating machine, and it considered as the granulation object with a particle diameter of about 200 micrometers. The approach of subsequent covering is optimum dose ****** about the precipitated calcium carbonate after carrying out like an example 1, carrying out a particle size regulation in the mesh of a 500-micrometer opening and considering as granular covering pharmaceutical preparation, Aspartame, and magnesium aluminometasilicate. (They are the amount of covering of the about 23 weight section, and particle diameter to the granulation object 100 weight section 0% 850 micrometers or more, and 0% 500 micrometers or more, and 1% 75 micrometers or less, mean-particle-diameter =260micrometer)

[0021]

[Example 3] The hydrochloric-acid ceftizoxime ARAPIBOKISHIRU 30 weight section, the precipitated-calcium-carbonate 30 weight section, and the crystalline cellulose 40 weight section were mixed, the after [granulation] particle size regulation was carried out with the dry type granulating machine, and it considered as the granulation object with a particle diameter of about 200 micrometers. It heat-treated at about 95 degrees C, having added the castor bean hardened-oil (melting point of 86 degrees C) 30 weight section to this granulation object 70 weight section, and mixing slowly by the agitation granulation in a plane, and cooling processing was carried out by taking out from an agitation granulation in a plane, and carrying out room temperature neglect after checking that melting was carried out enough and the granulation object has adhered at homogeneity. Furthermore, it heat-treated at about 75 degrees C, mixing slowly rapeseed hardened oil (melting point of 68 degrees C) to this granulation object 70 weight section covered once by 30 weight sections, in addition the agitation granulation in a plane, and cooling processing was carried out by taking out from an agitation granulation in a plane, and carrying out room temperature neglect after checking that melting was carried out enough and the granulation object has adhered at homogeneity. A particle size regulation is carried out in the mesh of a 500-micrometer opening after that, and it considers as granular covering pharmaceutical preparation, and is optimum dose ****** about Aspartame and magnesium aluminometasilicate. (They are the amount of covering of the about 104 weight section, and particle diameter to the granulation object 100 weight section 0% 850 micrometers or more, and 1% 500 micrometers or more, and 4% 75 micrometers or less, mean-particle-diameter =370micrometer)

[0022]

[Example 4] The hydrochloric-acid ceftizoxime ARAPIBOKISHIRU 30 weight section, the precipitated-calcium-carbonate 30 weight section, and the crystalline cellulose 40 weight section were mixed, the after [granulation] particle size regulation was carried out with the dry type granulating machine, and it considered as the granulation object with a particle diameter of about 200 micrometers. It heat-treated at about 95 degrees C, having added the castor bean hardened-oil (melting point of 86 degrees C) 5 weight section to this granulation object 95 weight section, and mixing slowly by the agitation granulation in a plane, and cooling processing was carried out by taking out from an agitation granulation in a plane, and carrying out room temperature neglect after checking that melting was carried out enough and the granulation object has adhered at homogeneity. Furthermore, it heat-treated at about 75 degrees C, mixing slowly rapeseed hardened oil (melting point of 68 degrees C) to this granulation object 95 weight section covered once by 5 weight sections, in addition the agitation granulation in a plane, and cooling processing was carried out by taking out from an agitation granulation in a plane, and carrying out room temperature neglect after checking that melting was carried out enough and the granulation object has adhered at homogeneity. A particle size regulation is carried out in the mesh of a 500-micrometer opening after that, and it considers as granular pharmaceutical preparation, and is optimum dose ****** about Aspartame and magnesium

aluminometasilicate. (They are the amount of covering of the about 11 weight section, and particle diameter to the granulation object 100 weight section 0% 850 micrometers or more, and 0% 500 micrometers or more, and 0% 75 micrometers or less, mean-particle-diameter =230micrometer)
[0023]
[Example 5] The hydrochloric-acid ceftizoxime ARAPIBOKISHIRU 30 weight section, the precipitated-calcium-carbonate 30 weight section, and the crystalline cellulose 40 weight section were mixed, the after [granulation] particle size regulation was carried out with the dry type granulating machine, and it considered as the granulation object with a particle diameter of about 200 micrometers. It heat-treated at about 95 degrees C, having added the castor bean hardened-oil (melting point of 86 degrees C) 10 weight section to this granulation object 90 weight section, and mixing slowly by the agitation granulation in a plane, and cooling processing was carried out by taking out from an agitation granulation in a plane, and carrying out room temperature neglect after checking that melting was carried out enough and the granulation object has adhered at homogeneity. Furthermore, it heat-treated at about 75 degrees C, mixing slowly rapeseed hardened oil (melting point of 68 degrees C) to this granulation object 90 weight section covered once by 10 weight sections, in addition the agitation granulation in a plane, and cooling processing was carried out by taking out from an agitation granulation in a plane, and carrying out room temperature neglect after checking that melting was carried out enough and the granulation object has adhered at homogeneity. Then, it is optimum dose ****** about Aspartame and magnesium aluminometasilicate further. (the granulation object 100 weight section -- receiving -- the amount of covering of the about 23 weight section, 2% of particle diameter of 850 micrometers or more and 3% 500 micrometers or more, and 1% 75 micrometers or less, and mean-particle-diameter =300micrometer)
[0024]
[Example 6] The hydrochloric-acid ceftizoxime ARAPIBOKISHIRU 30 weight section, the citric-acid 3 sodium 30 weight section, the crystalline cellulose 10 weight section (the Asahi Chemical Co., Ltd. make, trade name Avicel PH-302), and the ethyl cellulose 30 weight section (the Dow Chemical Co. make, trade name ethocell 10FP) were mixed, and by using dehydrated ethanol as joint liquid, after granulation, it dried, and the particle size regulation was carried out and it considered as the granulation object with a particle diameter of about 200 micrometers with the stirring granulator. It heat-treated at about 95 degrees C, having added the castor bean hardened-oil (melting point of 86 degrees C) 20 weight section to this granulation object 80 weight section, and mixing slowly with an agitation granulation machine, and cooling processing was carried out by taking out from an agitation granulation in a plane, and carrying out room temperature neglect after checking that melting was carried out enough and the granulation object has adhered at homogeneity. Next, it heat-treated at about 75 degrees C, mixing slowly rapeseed hardened oil (melting point of 68 degrees C) to this granulation object 90 weight section covered once by 10 weight sections, in addition the agitation granulation in a plane, and cooling processing was carried out by taking out from an agitation granulation in a plane, and carrying out room temperature neglect after checking that melting was carried out enough and the granulation object has adhered at homogeneity. Furthermore, it heat-treated at about 55 degrees C, having added the precipitated-calcium-carbonate 8 weight section, the sucrose-fatty-acid-ester (product [made from Mitsubishi Chemical Foods], trade name sugar ester P-1670) 10 weight section, and the Aspartame 2 weight section to this granulation object 80 weight section covered twice, and mixing slowly in a stirring granulator, and cooling processing was carried out by taking out from an agitation granulation in a plane, and carrying out room temperature neglect after checking that melting was carried out enough and the granulation object has adhered at homogeneity. A particle size regulation is carried out in the mesh of a 500-micrometer opening after that, and it considers as granular pharmaceutical preparation, and is optimum dose ****** about magnesium aluminometasilicate and perfume. (They are the amount of covering of the about 74 weight section, and particle diameter to the granulation object 100 weight section 0% 850 micrometers or more, and 0% 500 micrometers or more, and 3% 75 micrometers or less, mean-particle-diameter =300micrometer)
[0025]

[Example 7] The hydrochloric-acid ceftizoxime ARAPIBOKISHIRU 30 weight section, the precipitated-calcium-carbonate 30 weight section, the crystalline cellulose 10 weight section, and the ethyl cellulose 30 weight section were mixed, and by using dehydrated ethanol as joint liquid, after granulation, it dried, and the particle size regulation was carried out and it considered as the granulation object with a particle diameter of about 200 micrometers with the stirring granulator. It heat-treated at about 95 degrees C, having added the castor bean hardened-oil (melting point of 86 degrees C) 20 weight section to this granulation object 80 weight section, and mixing slowly with an agitation granulation machine, and cooling processing was carried out by taking out from an agitation granulation in a plane, and carrying out room temperature neglect after checking that melting was carried out enough and the granulation object has adhered at homogeneity. Next, it heat-treated at about 75 degrees C, mixing slowly rapeseed hardened oil (melting point of 68 degrees C) to this granulation object 90 weight section covered once by 10 weight sections, in addition the agitation granulation in a plane, and cooling processing was carried out by taking out from an agitation granulation in a plane, and carrying out room temperature neglect after checking that melting was carried out enough and the granulation object has adhered at homogeneity. Furthermore, it heat-treated at about 55 degrees C, having added the citric-acid 3 sodium 8 weight section, the sucrose-fatty-acid-ester 10 weight section, and the Aspartame 2 weight section to this granulation object 80 weight section covered twice, and mixing slowly in a stirring granulator, and cooling processing was carried out by taking out from an agitation granulation in a plane, and carrying out room temperature neglect after checking that melting was carried out enough and the granulation object has adhered at homogeneity. A particle size regulation is carried out in the mesh of a 500-micrometer opening after that, and it considers as granular pharmaceutical preparation, and is optimum dose ****** about magnesium aluminometasilicate and perfume. (They are the amount of covering of the about 74 weight section, and particle diameter to the granulation object 100 weight section 0% 850 micrometers or more, and 0% 500 micrometers or more, and 3% 75 micrometers or less, mean-particle-diameter =300micrometer)

[0026]

[Example 8] The milnacipran hydrochloride 30 weight section (a drug, product made from Pierre FABURU) and the crystalline cellulose 70 weight section were mixed, the after [granulation] particle size regulation was carried out with the dry type granulating machine, and it considered as the granulation object with a particle diameter of about 200 micrometers. The approach of subsequent covering is optimum dose ****** about Aspartame after carrying out like an example 1, carrying out a particle size regulation in the mesh of a 500-micrometer opening and considering as granular pharmaceutical preparation, magnesium aluminometasilicate, and citric-acid 3 sodium. (the granulation object 100 weight section -- receiving -- the amount of covering of the about 23 weight section, 0% of particle diameter of 850 micrometers or more and 0% 500 micrometers or more, and 1% 75 micrometers or less, and mean-particle-diameter =240micrometer)

[0027]

[Example 9] The milnacipran hydrochloride 30 weight section and the crystalline cellulose 70 weight section were mixed, the after [granulation] particle size regulation was carried out with the dry type granulating machine, and it considered as the granulation object with a particle diameter of about 200 micrometers. The approach of subsequent covering is optimum dose ****** about Aspartame after carrying out like an example 3, carrying out a particle size regulation in the mesh of a 500-micrometer opening and considering as granular pharmaceutical preparation, magnesium aluminometasilicate, and citric-acid 3 sodium. (the granulation object 100 weight section -- receiving -- the amount of covering of the about 104 weight section, 0% of particle diameter of 850 micrometers or more and 0% 500 micrometers or more, and 2% 75 micrometers or less, and mean-particle-diameter =360micrometer)

[0028]

[Example 10] The rokitamycin 30 weight section (a drug, Asahi Chemical Co., Ltd. make) and the crystalline cellulose 70 weight section were mixed, the after [granulation] particle size regulation was carried out with the dry type granulating machine, and it considered as the granulation object with a particle diameter of about 200 micrometers. The approach of subsequent covering is optimum dose

****** about Aspartame after carrying out like an example 1, carrying out a particle size regulation in the mesh of a 500-micrometer opening and considering as granular pharmaceutical preparation, magnesium aluminometasilicate, and citric-acid 3 sodium. (They are the amount of covering of the about 23 weight section, and particle diameter to the granulation object 100 weight section 0% 850 micrometers or more, and 0% 500 micrometers or more, and 1% 75 micrometers or less, mean-particle-diameter =220micrometer)

[0029]

[Example 11] The rokitamycin 30 weight section and the crystalline cellulose 70 weight section were mixed, the after [granulation] particle size regulation was carried out with the dry type granulating machine, and it considered as the granulation object with a particle diameter of about 200 micrometers. The approach of subsequent covering is optimum dose ****** about Aspartame after carrying out like an example 3, carrying out a particle size regulation in the mesh of a 500-micrometer opening and considering as granular pharmaceutical preparation, magnesium aluminometasilicate, and citric-acid 3 sodium. (the granulation object 100 weight section -- receiving -- the amount of covering of the about 104 weight section, 0% of particle diameter of 850 micrometers or more and 0% 500 micrometers or more, and 3% 75 micrometers or less, and mean-particle-diameter =330micrometer)

[0030]

[The example 1 of a comparison] The hydrochloric-acid ceftizoxime ARAPIBOKISHIRU 30 weight section, the precipitated-calcium-carbonate 30 weight section, and the crystalline cellulose 40 weight section were mixed, the after [granulation] particle size regulation was carried out with the dry type granulating machine, and it considered as the granulation object with a particle diameter of about 200 micrometers. It heat-treated at about 95 degrees C, having added the castor bean hardened-oil (melting point of 86 degrees C) 20 weight section to this granulation object 80 weight section, and mixing slowly by the agitation granulation in a plane, and cooling processing was carried out by taking out from an agitation granulation in a plane, and carrying out room temperature neglect after checking that melting was carried out enough and the granulation object has adhered at homogeneity. A particle size regulation is carried out in the mesh of a 500-micrometer opening after that, and it considers as granular pharmaceutical preparation, and is optimum dose ****** about Aspartame and magnesium aluminometasilicate. (They are the amount of covering of 25 weight sections, and particle diameter to the granulation object 100 weight section 0% 850 micrometers or more, and 0% 500 micrometers or more, and 1% 75 micrometers or less, mean-particle-diameter =260micrometer)

[0031]

[The example 2 of a comparison] The hydrochloric-acid ceftizoxime ARAPIBOKISHIRU 30 weight section, the precipitated-calcium-carbonate 30 weight section, and the crystalline cellulose 40 weight section were mixed, the after [granulation] particle size regulation was carried out with the dry type granulating machine, and it considered as the granulation object with a particle diameter of about 200 micrometers. It heat-treated at about 95 degrees C, having added the castor bean hardened-oil (melting point of 86 degrees C) 50 weight section to this granulation object 50 weight section, and mixing slowly by the agitation granulation in a plane, and cooling processing was carried out by taking out from an agitation granulation in a plane, and carrying out room temperature neglect after checking that melting was carried out enough and the granulation object has adhered at homogeneity. A particle size regulation is carried out in the mesh of a 500-micrometer opening after that, and it considers as granular pharmaceutical preparation, and is optimum dose ****** about Aspartame and magnesium aluminometasilicate. (They are the amount of covering of the 100 weight sections, and particle diameter to the granulation object 100 weight section 0% 850 micrometers or more, and 1% 500 micrometers or more, and 5% 75 micrometers or less, mean-particle-diameter =380micrometer)

[0032]

[The example 3 of a comparison] The hydrochloric-acid ceftizoxime ARAPIBOKISHIRU 30 weight section, the precipitated-calcium-carbonate 30 weight section, and the crystalline cellulose 40 weight section were mixed, the after [granulation] particle size regulation was carried out with the dry type granulating machine, and it considered as the granulation object with a particle diameter of about 200

micrometers. It heat-treated at about 75 degrees C, having added the rapeseed hardened-oil (melting point of 68 degrees C) 20 weight section to this granulation object 80 weight section, and mixing slowly by the agitation granulation in a plane, and cooling processing was carried out by taking out from an agitation granulation in a plane, and carrying out room temperature neglect after checking that melting was carried out enough and the granulation object has adhered at homogeneity. A particle size regulation is carried out in the mesh of a 500-micrometer opening after that, and it considers as granular pharmaceutical preparation, and is optimum dose ****** about Aspartame and magnesium aluminometasilicate. (They are the amount of covering of 25 weight sections, and particle diameter to the granulation object 100 weight section 0% 850 micrometers or more, and 0% 500 micrometers or more, and 1% 75 micrometers or less, mean-particle-diameter =260micrometer)

[0033]

[The example 4 of a comparison] The hydrochloric-acid ceftizoxime ARAPIBOKISHIRU 30 weight section, the precipitated-calcium-carbonate 30 weight section, and the crystalline cellulose 40 weight section were mixed, the after [granulation] particle size regulation was carried out with the dry type granulating machine, and it considered as the granulation object with a particle diameter of about 200 micrometers. 20 weight sections covering of the methylene chloride solution of castor bean hardened oil (melting point of 86 degrees C) was carried out with the fluid bed granulating machine (Powrex Make, trade name STREA-1) to this granulation object 80 weight section. A particle size regulation is carried out in the mesh of a 500-micrometer opening after that, and it considers as granular pharmaceutical preparation, and is optimum dose ****** about Aspartame and magnesium aluminometasilicate. (They are the amount of covering of 25 weight sections, and particle diameter to the granulation object 100 weight section 0% 850 micrometers or more, and 0% 500 micrometers or more, and 4% 75 micrometers or less, mean-particle-diameter =240micrometer)

[0034]

[The example 5 of a comparison] The hydrochloric-acid ceftizoxime ARAPIBOKISHIRU 30 weight section, the precipitated-calcium-carbonate 30 weight section, and the crystalline cellulose 40 weight section were mixed, the after [granulation] particle size regulation was carried out with the dry type granulating machine, and it considered as the granulation object with a particle diameter of about 200 micrometers. 20 weight sections covering of the ethanol solution of the ethyl cellulose which is a water-insoluble nature giant molecule was carried out with the fluid bed granulating machine to this granulation object 80 weight section. A particle size regulation is carried out in the mesh of a 500-micrometer opening after that, and it considers as granular pharmaceutical preparation, and is optimum dose ****** about Aspartame and magnesium aluminometasilicate. (They are the amount of covering of 25 weight sections, and particle diameter to the granulation object 100 weight section 0% 850 micrometers or more, and 0% 500 micrometers or more, and 4% 75 micrometers or less, mean-particle-diameter =220micrometer)

[0035]

[The example 6 of a comparison] The hydrochloric-acid ceftizoxime ARAPIBOKISHIRU 30 weight section, the precipitated-calcium-carbonate 30 weight section, and the crystalline cellulose 40 weight section were mixed, the after [granulation] particle size regulation was carried out with the dry type granulating machine, and it considered as the granulation object with a particle diameter of about 200 micrometers. It heat-treated at about 95 degrees C, having added the castor bean hardened-oil (melting point of 86 degrees C) 20 weight section to this granulation object 80 weight section, and mixing slowly by the agitation granulation in a plane, and cooling processing was carried out by taking out from an agitation granulation in a plane, and carrying out room temperature neglect after checking that melting was carried out enough and the granulation object has adhered at homogeneity. Furthermore, 10 weight sections covering of the ethanol solution of the ethyl cellulose which is a water-insoluble nature giant molecule was carried out with the fluid bed granulating machine to this granulation object 90 weight section covered once. A particle size regulation is carried out in the mesh of a 500-micrometer opening after that, and it considers as granular pharmaceutical preparation, and is optimum dose ****** about Aspartame and magnesium aluminometasilicate. (They are the amount of covering of the about 39

weight section, and particle diameter to the granulation object 100 weight section 0% 850 micrometers or more, and 1% 500 micrometers or more, and 3% 75 micrometers or less, mean-particle-diameter =280micrometer)

[0036]

[The example 7 of a comparison] The hydrochloric-acid ceftizoxime ARAPIBOKISHIRU 30 weight section, the precipitated-calcium-carbonate 30 weight section, and the crystalline cellulose 40 weight section were mixed, the after [granulation] particle size regulation was carried out with the dry type granulating machine, and it considered as the granulation object with a particle diameter of about 200 micrometers. It heat-treated at about 95 degrees C, having added the castor bean hardened-oil (melting point of 86 degrees C) 20 weight section to this granulation object 80 weight section, and mixing slowly by the agitation granulation in a plane, and cooling processing was carried out by taking out from an agitation granulation in a plane, and carrying out room temperature neglect after checking that melting was carried out enough and the granulation object has adhered at homogeneity. Furthermore, it heat-treated at about 95 degrees C, mixing slowly castor bean hardened oil (melting point of 86 degrees C) to this granulation object 80 weight section covered once by 20 weight sections, in addition the agitation granulation in a plane, and cooling processing was carried out by taking out from an agitation granulation in a plane, and carrying out room temperature neglect after checking that melting was carried out enough and the granulation object has adhered at homogeneity. A particle size regulation is carried out in the mesh of a 500-micrometer opening after that, and it considers as granular pharmaceutical preparation, and is optimum dose ****** about Aspartame and magnesium aluminometasilicate. (They are the amount of covering of 56 weight sections, and particle diameter to the granulation object 100 weight section 0% 850 micrometers or more, and 1% 500 micrometers or more, and 4% 75 micrometers or less, mean-particle-diameter =310micrometer)

[0037]

[The example 8 of a comparison] The milnacipran hydrochloride 30 weight section and the crystalline cellulose 70 weight section were mixed, the after [granulation] particle size regulation was carried out with the dry type granulating machine, and it considered as the granulation object with a particle diameter of about 200 micrometers. The approach of subsequent covering is optimum dose ****** about Aspartame after carrying out like the example 1 of a comparison, carrying out a particle size regulation in the mesh of a 500-micrometer opening and considering as granular pharmaceutical preparation, magnesium aluminometasilicate, and citric-acid 3 sodium. (the granulation object 100 weight section -- receiving -- the amount of covering of 25 weight sections, 0% of particle diameter of 850 micrometers or more and 0% 500 micrometers or more, and 1% 75 micrometers or less, and mean-particle-diameter =230micrometer)

[0038]

[The example 9 of a comparison] The milnacipran hydrochloride 30 weight section and the crystalline cellulose 70 weight section were mixed, the after [granulation] particle size regulation was carried out with the dry type granulating machine, and it considered as the granulation object with a particle diameter of about 200 micrometers. The approach of subsequent covering is optimum dose ****** about Aspartame after carrying out like the example 4 of a comparison, carrying out a particle size regulation in the mesh of a 500-micrometer opening and considering as granular pharmaceutical preparation, magnesium aluminometasilicate, and citric-acid 3 sodium. (the granulation object 100 weight section -- receiving -- the amount of covering of 25 weight sections, 0% of particle diameter of 850 micrometers or more and 0% 500 micrometers or more, and 5% 75 micrometers or less, and mean-particle-diameter =230micrometer)

[0039]

[The example 10 of a comparison] The rokitamycin 30 weight section and the crystalline cellulose 70 weight section were mixed, the after [granulation] particle size regulation was carried out with the dry type granulating machine, and it considered as the granulation object with a particle diameter of about 200 micrometers. The approach of subsequent covering is optimum dose ****** about Aspartame after carrying out like the example 1 of a comparison, carrying out a particle size regulation in the mesh of a

500-micrometer opening and considering as granular pharmaceutical preparation, magnesium aluminometasilicate, and citric-acid 3 sodium. (They are the amount of covering of 25 weight sections, and particle diameter to the granulation object 100 weight section 0% 850 micrometers or more, and 0% 500 micrometers or more, and 1% 75 micrometers or less, mean-particle-diameter =210micrometer)
[0040]
[The example 11 of a comparison] The rokitamycin 30 weight section and the crystalline cellulose 70 weight section were mixed, the after [granulation] particle size regulation was carried out with the dry type granulating machine, and it considered as the granulation object with a particle diameter of about 200 micrometers. The approach of subsequent covering is optimum dose ****** about Aspartame after carrying out like the example 4 of a comparison, carrying out a particle size regulation in the mesh of a 500-micrometer opening and considering as granular pharmaceutical preparation, magnesium aluminometasilicate, and citric-acid 3 sodium. (They are the amount of covering of 25 weight sections, and particle diameter to the granulation object 100 weight section 0% 850 micrometers or more, and 0% 500 micrometers or more, and 5% 75 micrometers or less, mean-particle-diameter =210micrometer)
[0041]
[The example 1 of a trial] I had five health adults include 0.5g of granular pharmaceutical preparation manufactured in examples 1-11 and the examples 1-11 of a comparison in opening (on a tongue), and organic-functions evaluation 20 - 30 seconds after was performed. tasteless [to the taste] as the approach of evaluation -- it divides into five steps ((0), (1) which sense bitterness small, (2) which sense the bitterness of extent which is not sensed as dysphoria, (3) which sense the bitterness of extent sensed as dysphoria, and (4) it is sensed that are very bitter), and smooth to a rough deposit -- it divided into two steps ((0), and rough (1)), and the sum total of evaluation of five persons compared.
[0042]
[Table 1]

味	被験者A	被験者B	被験者C	被験者D	被験者E	Total
実施例1	1	0	1	0	1	3
実施例2	1	0	0	0	1	2
実施例3	0	0	0	0	0	0
実施例4	1	0	1	0	2	4
実施例5	1	0	0	0	1	2
実施例6	1	0	0	0	1	2
実施例7	0	0	0	0	1	1
比較例1	3	2	3	2	4	14
比較例2	2	2	3	1	3	11
比較例3	3	2	4	2	4	15
比較例4	4	3	4	3	4	18
比較例5	4	3	4	4	4	19
比較例6	2	2	2	3	3	12
比較例7	2	2	2	1	2	9
実施例8	0	0	0	0	1	1
実施例9	0	0	0	0	0	0
比較例8	2	2	3	2	3	12
比較例9	4	3	4	3	4	18
実施例10	0	0	1	0	1	2
実施例11	0	0	0	0	0	0
比較例10	1	2	2	2	3	10
比較例11	2	3	3	2	4	14

[A continuation of Table 1]

きらつき	被験者A	被験者B	被験者C	被験者D	被験者E	Total
実施例1	0	0	0	0	0	0
実施例2	0	0	0	0	0	0
実施例3	1	1	1	0	1	4
実施例4	0	0	0	0	0	0
実施例5	1	1	1	1	1	5
実施例6	0	0	0	0	0	0
実施例7	0	0	0	0	0	0
比較例1	0	0	0	0	0	0
比較例2	1	1	0	1	1	4
比較例3	0	0	0	0	0	0
比較例4	1	1	1	1	1	5
比較例5	1	1	1	0	1	4
比較例6	0	1	1	0	1	3
比較例7	1	1	0	0	1	3
実施例8	0	0	0	0	0	0
実施例9	1	1	0	1	1	4
比較例8	0	0	0	0	0	0
比較例9	0	1	1	0	1	3
実施例10	0	0	0	0	0	0
実施例11	0	0	0	1	1	2
比較例10	0	0	0	0	0	0
比較例11	0	0	1	0	1	2

[0043] Consequently, the following thing became clear.
1) The examples 1-7 of the masking effect of the taste are clearly higher than one to examples 1-7 and example of comparison 7 comparison.
2) The example of the masking effect of the taste is clearly higher than the comparison of examples 8 and 9 and the examples 8 and 9 of a comparison.
3) The example of the masking effect of the taste is clearly higher than the comparison of examples 10 and 11 and the examples 10 and 11 of a comparison.
4) When the amount of covering of the example [an example and] of a comparison increases, they have the inclination for a masking effect to increase.
5) Although examples 1, 2, 4, and 5 had few amounts of covering compared with the example 7 of a comparison, its masking effect of the taste was remarkably high.
6) An example and the example of a comparison tend to be rough when the amount of covering increases.
7) From the comparison of an example 1 and an example 5, there is an inclination which is rough if a mesh is not bet.
8) What was covered with the fluid bed tends to be rough from the examples 4, 5, 6, 8, and 11 of a comparison. .
[0044]
[The example 2 of a trial] It is Japanese pharmacopoeia General Test Procedures about the granular pharmaceutical preparation manufactured in examples 1-7 and the examples 1-7 of a comparison. Dissolution test The rate of elution when feeding the drug of 100mg considerable amount into the buffer solution (it being 37 degrees C whenever [pH 1.2 / about / and solution temperature] with the liquid which melted dilute-hydrochloric-acid 24.0mL and water to 2.0g of sodium chlorides, and was set to 1000mL(s)) of 900mL(s) according to the 2nd law (a paddle method, paddle rotational frequency 50 rotation) was measured till after [an injection] 60 minutes.
[0045] Consequently, 80% or more of rate of elution has elution in 30 minutes early from drawing 1 except example 3 and example of comparison 2.

[0046] From the result of the examples 1 and 2 of an experiment, by using for order with the high melting point two or more kinds of support whose melting points are 40 degrees C - 90 degrees C, the masking effect of the taste increases and it is guessed by controlling the addition that the rate of elution is also controllable.

[0047]

[Effect of the Invention] In order that the granular covering pharmaceutical preparation of this invention may cover two or more kinds of support, masking effect sufficient with a little addition is acquired. Moreover, the elution nature in extent (is it made masking after suspension for how many hours?) and alimentary canal of masking can be adjusted by adjusting the class, the ratio, and the amount of covering of the support to cover. Therefore, it can respond to various pharmaceutical preparation, such as dry-syrups, powder, and a granule, and the optimal particle diameter, coating thickness, etc. can be chosen and controlled. Moreover, in order not to use an organic solvent, since the covering approach is also easy, industrialization is easy [it is safe and environment-friendly, and].

[Translation done.]

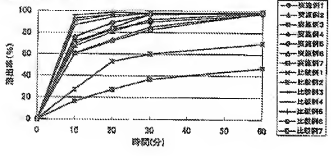
DESCRIPTION OF DRAWINGS

[Brief Description of the Drawings]
[Drawing 1] The rate of elution of the drugs by the example 2 of a trial is shown.

[Translation done.]

DRAWINGS

[Drawing 1]



[Translation done.]